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10/763,876	01/23/2004	Abraham J. Domb	PG 102	6009

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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	PAPER NUMBER
1618	
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/763,876	DOMB, ABRAHAM J.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 February 2008*.

2a)☒ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The examiner acknowledges receipt of request for extension of time, request for continued examination under 37 CFR 1.114, amendment and remarks, all filed 08/18/08. Claims 1 and 4 are amended. New claims 15-24 are added. Therefore, claims 1-10 and 15-24 are pending.

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 8/18/08 has been entered.

Specification

2. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: The recitation in claims 8 and 22 that ricinoleic acid comprises at least 90% by weight of the polymer does not derive antecedent support from the disclosure. While original claim 8 has that language, the disclosure does not provide support. Correction is respectfully requested.

Response to Arguments

Previous rejections that are not reiterated herein are withdrawn.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 6, 7 and 15-24 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

5. For claims 6 and 15 recite "derivatives," an the boundaries of the ester derivatives or derivatives are not defined.

Response to Arguments

6. Applicant's arguments filed 2/04/2008 have been fully considered but they are not persuasive. Please note that applicant did not provide any arguments traversing the rejection of the use of derivatives in the claims with no clear limits of what those derivatives are. However, the response to the arguments of 02/04/08 is reproduced below.

7. Applicant argued on 02/04/08 that ester derivative is clear because ester derivative of ricinoleic acid is when either of the two functionalities on the acid is esterified, but the meets and bound of that derivative is not known. It was brought to applicant's attention that the specification at paragraph [0049] says that an example of non-linear fatty acid derivative is ricinoleic acid and it is unclear where the boundaries of the ester derivative of ricinoleic acid would be and although applicant talks about esterified functionality on the ricinoleic acid, applicant did not name any of those derivatives. The issue in not just the clarity of what an ester

derivative of ricinoleic acid would be but the meets and bounds of those derivatives. Correction is respectfully requested.

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 15-21 and 24 are rejected under 35 U.S.C. 102(b) as being anticipated by Domb et al. (US 5,473,103).

10. Domb describes polyester anhydrides derived from ricinoleic acid and sebacic acid (column 2, lines 60-62) for encapsulation and subsequent release of agents such as drugs, peptides, antibodies (column 5, lines 4, 17, 18, 23-28, 35-38), meeting claims 15-18 and 20. Ciprofloxacin disclosed in Fig. 2 meets claim 24. Claims 19 and 22 are product by process claims and are thus met by the product of the prior art. Claim 21 says it is suitable for injection reading on a product that would be suitable for injection. The product of the prior art would also be suitable for injection noting that the claim did not claim any form.

11. Claims 1 and 8 are rejected under 35 U.S.C. 102(b) as being anticipated by Storey et al. (US 5,756,652).

12. Storey discloses a biodegradable poly(ester anhydride) that are used in medical implants for the release of bioactive substances (abstract; column 1, lines 6-11; column 5, lines 15-22) meeting claim 1. Claim 8 is product by process claim and the claim is thus met by the product

of Storey. However, Storey synthesizes the poly(ester anhydride) from carboxy-terminated and bis-carboxy-terminated polyesters (abstract; column 1, lines 6-11; column 2; column 3, lines 57-65). It is noted that Storey does not exclude the ester moiety from being random so that randomness of the ester bond would be inherent (see column 7, lines 16-43)

13. Claims 1-8 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by or in the alternative, under 35 U.S.C. 103(a) as obvious over Teomim et al. ("Ricinoleic acid-based biopolymers" in the Journal of Biomedical Materials Research, Vol. 45, Issue 3, pages 258-267, John Wiley & Sons, Inc.) or Domb et al. ("Biopolymers as drug carriers and bioactive macromolecules" in Acta Polymerica, 14 Dec. 1998, Volume 49, Issue 10-11, Pages 526 - 533).

Teomim discloses ricinoleic passed biopolymer derived from ricinoleic acid and maleic or succinic anhydride for the delivery of methotrexate, an anticancer agent (pages 258-267). The methotrexate meets claims 2 and 10. Ricinoleic acid meets the requirements of claims 1, 4, 5 and 8. The succinic anhydride or succinate meets claim 6. Since the composition of Teomim is the same composition as the composition in claim 1, it flows that the composition of Teomim would also be "suitable for administration by injection" as recited in claim 3. The polyanhydride polymer of Teomim contains ester bonds (see structure in Table 1 of page 263). Teomim is silent about the randomness of the ester bonds. Thus, in the alternate, since Teomim is silent as to the randomness of the ester bond within the polymer, the randomness of the ester bond within the polymer would be obvious because the preparation method does not exclude randomness of the bonds and applicant has not factually shown that the bonds in the polymer of Teomim are not random and that ester bonds are absent in the polyanhydride polymer of Teomim. Claim 8 is product by process claim and the claim is thus met by the product of Teomim.

Domb described biodegradable polyanhydrides derived from ricinoleic acid sebacic acid as drug carriers with nystatin, amphotericin B as small molecules drugs disclosed in the manuscript (pages 526-533). Since the composition of Domb is the same composition as the composition in claim 1, it flows that the composition of Domb would also be "suitable for administration by injection" as recited in claim 3. Specifically, Domb on page 530, left column at the 3rd full paragraph indicates that the polymer is a copolyester-anhydride. Domb is however silent as to the random nature of the of the ester bond in the polymer. But since Domb prepares the polymer by combining ricinoleic acid and maleic anhydride or succinic anhydride just as the polymer is instantly prepared in paragraph [0127], it would flow that the ester bonds are random. However, in the alternate, since Domb is silent as to the randomness of the ester bond within the polymer, the randomness of the ester bond within the polymer would be obvious because the preparation method does not exclude randomness of the bonds and applicant has not factually shown that the bonds in the polymer of Domb are not random and that ester bonds are absent in the polyanhydride polymer of Domb. Claim 8 is product by process claim and the claim is thus met by the product of Domb.

Claim Rejections - 35 USC § 103

14. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

15. Claims 1, 2, 3, 9 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Storey et al. (US 5,756,652) in view of Gander et al. (US 5,648,096) or Brem et al. (US 5,626,862).

Storey discloses the use of polyester anhydride as an implant for delivery of bioactive substances (abstract; column 1, lines 6-11; column 5, lines 15-22). Storey does not name any specific bioactive substances. But it is known that many bioactive substances are delivered by implant to the desired sites. For example, Gander describes that biodegradable microcapsules are useful in the delivery of bioactive substances as implants and perenterally administrable microparticles using biodegradable polymers (column 1, lines 28, 29, 35-42). Gander further microcapsules that can include low molecular weight active materials (column 6, lines 7-28), nonsteroidal anti-inflammatory drugs (column 6, lines 29-54), sex hormones (column 6, line 55 to column 7, line 3), and antihistamines (column 7, lines 4-57), with these drugs meeting the limitations of the bioactive agents of claims 2 and 10, the administration mode of parenteral or injection meeting claim 3, and the microparticles meeting claim 9.

Also Brem discloses the use of polymeric implant such as microimplants where microparticles, microspheres and microcapsules encapsulate the drugs (column 11, lines 19-28) with the microparticles meeting claim 9, for the delivery of drugs like anticancer drugs such as paclitaxel and camptothecin (abstract; column 7, lines 19 and 20; column 3, lines 64-67; column 5, lines 8-16) with the anti cancer drugs meeting claims 2 and 10; the drug can be encapsulated within the polymer (column 5, lines 18-20) meeting claim 9; the drug can be administered by subcutaneous injection and/or implantation (column 8. lines 53, 59) meeting claim 3.

Therefore, taking the teachings of the references together, the person of ordinary skill at the time the invention was made would have reasonable expectation of success that the biologically active agents of Brem or Gander would be effectively delivered when incorporated in the polymeric device of Storey.

16. Claims 1 and 8 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teomim et al. ("Ricinoleic acid-based biopolymers" in the Journal of Biomedical Materials Research, Vol. 45, Issue 3, pages 258-267, John Wiley & Sons, Inc.) or Domb et al. ("Biopolymers as drug carriers and bioactive macromolecules" in Acta Polymerica, 14 Dec. 1998, Volume 49, Issue 10-11, Pages 526 - 533).

Teomim and Domb are discussed above as meeting the requirements of claim 1. While claim 8 is a product by process claim, it is noted neither reference specifically discloses the recited %amount of the ricinoleic acid relative to the polymer that would produce the desired polymer that would provide the desired release of the active agent. But, the artisan has the technical skills to determine how much ricinoleic acid is present within the polymer. Therefore, taking the teachings of the references, one having ordinary skill in the art would expect that using polymer having appropriate %amount of ricinoleic acid would provide a polymer delivery device that would effectively deliver drugs/active agent and in the absence of factual showing, the recited %amount of the ricinoleic acid is not inventive over a prior art reference that describes the same composition that is used as drug carrier and that is silent on the amount of the fatty acid.

17. Claims 1 and 9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Teomim et al. ("Ricinoleic acid-based biopolymers" in the Journal of Biomedical Materials Research,

Vol. 45, Issue 3, pages 258-267, John Wiley & Sons, Inc.) or Domb et al. ("Biopolymers as drug carriers and bioactive macromolecules" in Acta Polymerica, 14 Dec. 1998, Volume 49, Issue 10-11 , Pages 526 - 533).

Teomim and Domb are described above as anticipating claim 1. Both Domb and Teomim are silent on the particulate nature of the composition. It is known in the art that particles used as drug carriers have the advantage of high stability, high carrier capacity in view of the large surface area, possibility of incorporation of hydrophobic and hydrophilic substances, capacity for sustained release and ability for use in variable routes of administration including oral, parenteral and inhalation, all of which aid bioavailability and uptake of active substances by the target sites. Therefore, it would be obvious to prepare the composition of Domb or Teomim in particulate form, microparticle or nanoparticle, with the expectation of deriving the advantages of the use of particles in drug delivery.

Response to Arguments

18. Applicant's arguments filed 08/18/08 have been fully considered but they are not persuasive.

19. *Regarding Storey*: In response to applicants arguments a) that Storey does not disclose random ester bonds in the polymer backbone, it is noted that because Storey does not teach that the ester bond in the backbone of the polymer cannot be or are not random. If applicant so believes they are not, the burden is on the applicant to factually show that the ester bonds in Storey are not random but .... b) In response to applicants statement that figs. 1 and 6 show that the ester bonds are at regular intervals in the polyester blocks but applicant has not pointed to applicants polyester blocks having the random ester bonds. c) In response to applicants

assertion that random bonds cannot be inherently taught by Storey, it is noted and applicant does not show where in Storey is taught that the ester bonds are not random, it is also noted that applicant has not provided the structure of applicant's polyester anhydride showing random intervals of the ester bonds in the backbone. It is also noted that the figures referred to by applicant are not the only exemplification of polymerization reactions in Storey. Opinion representation does not take the place of factual showing. Please note that that claims 6, 7, 15 and 16 have not now been rejected over Storey, and in that wise arguments against Storey in view of claims 6, 7, 15 and 16 ands 17-24 are moot.

20. *Also regarding Storey in view of Gander or Brem*: Applicant's argument that Storey does not teach polymers having random ester bonds along the backbone is not persuasive because there is no teaching in Storey that the polymer does not contain random ester bonds and applicant has not factually shown that the ester bonds in Storey are not random.

21. *Regarding Griffin*: Applicants arguments with respect to Griffin are moot because the rejection is not made now.

22. *Regarding Teomim*: In response applicant's arguments that Teomim does not disclose poly(ester-anhydride), it is noted that the polymer on page 263 of Teomim shows the presence of ester bonds. The examiner further disagrees with the applicant as to the method of preparation of the polyester anhydride contributing to structure that is different from that of Teomim because, the claim is not directed to the method of preparing the polyester anhydride and the limitations that applicant argues about are not in the claims. While Teomim may produce the polyanhydride by melt polymerization, applicant has not provided factual evidence that melt polymerization would lead to polymer that would exclude the presence of ester bonds in the

polymer or the presence of random ester bonds in the polymer. In response to applicant's argument that the ordinary skilled artisan would not have been motivated to modify the polyanhydride of Teomim, it is noted that modification of the polyanhydride of Teomim in terms of random or regular ester bonds and in terms of liquid or solid nature of the polymer, it is noted that claim 1 does not recite a liquid formulation, the polymer of Teomim has random ester bonds as described above, claim 8 is product by process claim that reads on the product of Teomim. Please note that that claims 15-24 have not now been rejected over Teomim and in that wise arguments against Teomim in view of claims 15-24 are moot.

23. *Regarding Domb*: Please note that that claims 15 and 16 have not now been rejected over Domb, and in that wise arguments against Domb in view of claims 15 and 16 and 17-24 are moot. In response to applicant's arguments that Domb's polymers do not contain ester bonds, it is noted that mixing/reacting of the ricinoleic acid and the anhydrides would lead to a polymer structure having random ester bonds. Furthermore, applicant has not factually shown that the polymer of Domb does not have an ester bond or does not have random ester bond. Domb on page 530, left column at the 3rd full paragraph names the polymer as a copolyester-anhydride. In response to applicant's arguments that the block copolymer of Domb is structurally different from the claimed polymer, it is noted that applicant has not factually shown how the claimed polymer structurally differs form the disclosed polymer. The examiner states that the examiner alleges that randomness of the ester bond within a polymer would be obvious. The examiner disagrees with applicant's characterization that to say that the prior art, in this case, the Domb reference does not teach ester bonds that are not random is an allegation is just not the case

because no where in the Domb reference is there a disclosure that the ester bonds are regular or random. Applicant has not provided any factual showing that the bonds in Domb cannot ever be random. Furthermore, a structural alteration is not required to render claim 9 or 8 obvious according to the rejections and responses on record here.

24. Claims 15, 19 and 21-23 are rejected under 35 U.S.C. 103(a) as being unpatentable over Domb et al (US 5,473,103) in view of O'Hagan (Advanced Drug Delivery Reviews, 1 Dec. 1998, pages 305-320).

25. Domb is described above. Claim 19 is product by process claim and thus reads on the product of Domb. However, it would also be obvious for the artisan to use the linoleic acid and the sebacic acid in amounts relative to each during the preparation step that would lead to as polyester anhydride polymer that would be suitable for entrapping drugs that would eventually be released. Regarding claim 21, suitable for injection is the route of administering the product and suitable the product of the prior art would also be suitable for injection in the appropriate form. Claim 22 is also a product by process claim and the artisan has the technical skills to use the chemistry to arrive at a product that would have at least 90% by weight of the polymer.

26. Domb does not disclose that the active agent is encapsulated in microparticles. But it is known that use of microparticles in drug delivery improves bioavailability (see O'Hagan, the whole reference and the abstract). Therefore, one having ordinary skill in the art at the time the invention was made would be motivated to use particles for the encapsulation of the drugs in order to achieve improved bioavailability. within the technical skill of the artisan to use amounts of ricinoleic acid and sebacic acid

27. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Blessing M. Fubara/
Examiner, Art Unit 1618